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Serum albumin level in critically ill pediatric patients

Gurkan Atay, Seher Erdoğan
Department of Pediatric Critical Care, Health Science University, Umraniye Research and Training Hospital, İstanbul, Turkey

Abstract
Aim: Hypoalbuminemia is a frequent condition among patients admitted to the pediatric intensive care unit (PICU). The aims of the present study were to determine the prevalence of hypoalbuminemia among critically ill pediatric patients and assess its relationship with prognosis.
Material and Methods: This was a retrospective observational study evaluating the albumin levels and prognoses recorded among patients admitted to the PICU between May 2017 and December 2018. The patients were categorized into two groups; those with hypoalbuminemia were assigned to Group 1.
Results: The study enrolled a total of 126 pediatric patients, of whom 64 (50.8%) were female. One hundred and five (83.3%) patients survived and 21 (16.7%) died. Forty-six (36.5%) patients had hypoalbuminemia. Among the patients assigned to Group 1, the need for mechanical ventilation (MV) was significantly greater (p=0.007), but there was no significant difference between the number of days of MV (p=0.64). Group 1 had significantly greater PRISM scores, significantly longer hospital stays, and a significantly higher mortality rate (p=0.000, p=0.013, and p=0.000, respectively). No significant difference was seen for the number of days spent in the PICU. Prognosis analysis revealed that surviving patients had a higher mean age, less need for MV, shorter hospitalization and MV times, and lower serum total protein and albumin levels.
Discussion: We suggest that serum albumin level is an important prognostic marker as it is a simple, specific, and low-cost parameter that is routinely used in most PICUs.

Keywords
Hypoalbuminemia, Pediatric, Intensive Care, Mortality

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Corresponding Author: Seher Erdoğan, Department of Pediatric Critical Care, Health Science University, Umraniye Research and Training Hospital, İstanbul, Turkey.
E-mail: seher70@gmail.com P: +90 532 667 83 70
Corresponding Author ORCID ID: https://orcid.org/0000-0002-3393-3363

Introduction

Albumin has a long half-life of 15-19 days. Among critically ill patients, however, serum albumin levels may rapidly drop within 3-5 days. Albumin plays many physiological roles including the regulation of colloid osmotic pressure; binding and transport of various substances in the blood, such as drugs and hormones; contributions of antioxidant properties; and nitric oxide modulation [1]. Inflammatory processes increase albumin catabolism and may reduce its production. During critical illnesses, capillary permeability is dramatically reduced, leading to albumin exchange between the intravascular and extravascular compartments [2-4]. Previous studies have shown a hypoalbuminemia prevalence of 21-76% among critically ill children [5-7]. The aim of the present study was to determine the prevalence of hypoalbuminemia and its relationship with prognosis among children admitted to a pediatric intensive care unit (PICU).

Material and Methods

This study was approved by the local ethics committee of Ümraniye Training and Research Hospital. It was conducted retrospectively in a 10-bed PICU. Age, sex, admission diagnosis, Pediatric Risk of Mortality (PRISM) score, serum total protein and albumin levels, mechanical ventilation (MV) need, number of days on MV, number of days in the PICU, number of days in the hospital, and prognosis were recorded for all patients admitted to the PICU between May 2017 and May 2018.

Patients with nephrotic syndrome, liver cirrhosis, protein energy malnutrition, burns, recent cardiovascular surgery, and various disorders that might potentially affect serum albumin level were excluded in addition to those who received parenteral nutrition and albumin infusion prior to admission. Hypoalbuminemia was defined as a serum albumin level of ≤2.5 g/dL among patients younger than 7 months and ≤3.4 g/dL among older ones. The patients were assigned to two separate groups, Group 1 and Group 2, indicating hypoalbuminemia and normal serum albumin levels, respectively. Written informed consent was not obtained from the parents and guardians of the patients included in this study since the study is a retrospective study and data were obtained by the screening of patient files.

Statistical Analysis

The study data were analyzed using the IBM SPSS Statistics 22 software package (IBM SPSS, Turkey). The normality of data distribution was tested with the Shapiro-Wilk test; the descriptive statistics included mean, standard deviation, and frequency. The Student t-test was used for comparison of normally distributed quantitative data and the Mann-Whitney U test for non-normally distributed data. Qualitative data were compared with Yates continuity correction. Statistical significance was set at $p<0.05$.

Results

During the study period 154 patients were admitted; 28 patients not meeting the inclusion criteria were excluded. There were 64 (50.8%) female and 62 (49.2%) male patients, with a total of 126 pediatric patients included in the study. The mean age was 64.66±71.28 months. The mean serum total protein level was 5.84±1.11 (min-max: 3.4-8), while mean albumin level was 3.63±0.59 (min-max: 2.1-4.9). Fifty-three (42.1%) patients received respiratory support via MV. The mean PRISM score was 11.8±10.3, the mean number of days on MV was 25.6±30.9, the mean duration of PICU stay was 17.6±24.0 days, and the mean duration of hospital stay was 23.5±25.9 days. While 105 (83.3%) patients survived, 21 (16.7%) patients died. Forty-six (36.5%) patients had hypoalbuminemia (Table 1).

The female patients had a higher rate of hypoalbuminemia (p=0.03), and the mean age of patients in Group 1 was younger, but that difference did not reach statistical significance. Among

Table 1. Demographic characteristics of the study population

Variable	
Age (months), median (IQR)	34 (2-250)
Number of days in PICU, median (IQR)	7 (2-132)
Number of days in hospital, median (IQR)	14 (3-143)
PRISM score, median (IQR)	8.5 (1-49)
MV days, median (IQR)	8 (1-130)
Total protein, median (IQR)	5.9 (3.4-8.0)
Albumin, median (IQR)	3.6 (2.1-4.9)
Sex, female, n (%)	50.8 (64)
MV need, n (%)	42.1 (53)
Prognosis, survived, n (%)	105 (83.3)
Hypoalbuminemia, n (%)	46 (36.5)

PICU: Pediatric intensive care unit, PRISM: Pediatric Risk of Mortality, MV: mechanical ventilation.

Table 2. Comparison of Group 1 and Group 2

	Group 1	Group 2	p
Age (months), median (IQR)	56 (3-227)	2 (2-250)	0.067*
Duration of PICU stay (days), median (IQR)	10 (2-78)	6 (2-132)	0.100*
Duration of hospital stay (days), median (IQR)	21 (3-83)	10 (3-43)	0.002*
PRISM score, median (IQR)	14 (2-49)	7 (1-40)	0.004*
MV days, median (IQR)	7.5 (1-78)	8 (1-130)	0.79*
Total protein (g/dL), median (IQR)	5.1 (3.4-7.5)	6 (3.4-8.0)	<0.001*
Serum albumin (g/dL), median (IQR)	3 (2.1-3.4)	3.9 (2.7-4.9)	<0.001*
Sex, female, n (%)	17 (37%)	47 (58.8%)	0.030+
MV need, n (%)	27 (58.7%)	26 (32.5%)	0.007+
Prognosis, survived, n (%)	30 (65.2%)	75 (93.8%)	<0.001+

*Mann-Whitney U test; +Yates continuity correction PICU: Pediatric intensive care unit, PRISM: Pediatric Risk of Mortality, MV: mechanical ventilation.

Table 3. Comparison of study parameters by prognosis

Variable	Prognosis		p
	Survived	Deceased	
Age (months), median (IQR)	37 (2-250)	6 (2-203)	0.017*
Duration of PICU stay (days), median (IQR)	5 (2-132)	38 (2-85)	0.001*
Duration of hospital stay (days), median (IQR)	14 (3-141)	38 (3-85)	0.060*
PRISM score, median (IQR)	6 (1-49)	24 (10-49)	<0.001*
MV days, median (IQR)	6 (1-130)	35 (2-80)	0.020*
Total protein (g/dL), median (IQR)	6 (4.3-8)	5 (3.4-7.5)	0.001*
Serum albumin (g/dL), median (IQR)	3.7 (2.1-4.9)	3 (2.4-4.1)	<0.001*
Sex, female, n (%)	56 (53.3%)	8 (38.1%)	0.300+
MV need, n (%)	32 (30.5%)	21 (100%)	<0.001+

*Mann-Whitney U test, +Yates continuity correction, PICU: Pediatric intensive care unit, PRISM: Pediatric Risk of Mortality, MV: mechanical ventilation.

patients in Group 1, the need for MV was significantly greater although the numbers of days on MV were similar. The patients in Group 1 had higher PRISM scores, longer hospital stays, and higher mortality rate (p=0.000, p=0.013, and p=0.000, respectively). The numbers of days spent in the PICU were similar (Table 2).

As for prognosis, the surviving patients had higher mean age, less need for MV, shorter durations of PICU stay and MV use, and higher serum total protein and albumin levels (Table 3).

Discussion

Our study showed a hypoalbuminemia prevalence of 36% at admission among patients admitted to the PICU. Like previous studies, patients with hypoalbuminemia had greater need for MV, higher PRISM scores, longer hospital stays, and higher mortality rates than those with normal albumin levels [7-10].

In a study from 2016 involving 202 critically ill children, the prevalence of hypoalbuminemia was found to be 57.9%. Those patients had longer PICU stays and MV requirements as well as a mortality rate four times higher than that of children with normal albumin levels. Likewise, our study demonstrated greater mortality among patients with hypoalbuminemia. Although there was a greater need for MV, the duration of MV use was not significantly different between the study groups, but the duration of hospital stay was prolonged in Group 1. Patients in that group were younger, but the age difference did not reach statistical significance [8].

Durward et al. [9], in a similar study, reported a hypoalbuminemia prevalence of 57% at admission, which rose to 76% after 24 hours. They suggested that that increase may have been due to a decrease in albumin synthesis capacity and the very low rate of use of albumin as a volume expander in their unit. There was no correlation between mortality and hypoalbuminemia at admission or the 24th hour, but they reported that PICU stays were longer in patients with hypoalbuminemia (4.9 vs. 3.6 days). They suggested that patients with extreme hypoalbuminemia constituting a minority resulted in that finding.

Tiwari et al. [10] reported that 21% of 435 critically ill children had hypoalbuminemia at admission, with that rate rising to 34% by the end of the first week and 37% during the whole period of PICU follow-up. Those patients had higher PRISM scores (12.9 vs. 7.5), longer PICU stays (13.8 vs. 6.7 days), greater MV needs, longer MV usage (p<0.001), and a higher mortality rate (87.8% vs. 16.2%). This effect of albumin on mortality does not solely depend on its regulatory effect on colloid osmotic pressure and capillary permeability, but also on binding lipids and drugs as well as providing a means for transport of trace elements such as copper and zinc in the circulation [11].

The indications for albumin treatment include hypovolemia, shock, burns, hypoalbuminemia, surgery and trauma, acute respiratory distress syndrome, plasmapheresis, and hemodialysis. In critically ill patients who may have endothelial injury, treatment with colloids and crystalloids may increase interstitial fluid volume [12, 13]. In the SAFE (Saline versus Albumin Fluid Evaluation) study [14] comprising 6997 patients, 4% albumin or saline was administered when there was a need for fluids. That study demonstrated no significant difference between the mortality rates of the groups. A subgroup analysis revealed that albumin was beneficial in severe sepsis but detrimental in traumatic brain injury. The EARSS study [15], a randomized and controlled multicenter study, compared patients with early severe sepsis who were administered normal saline or 100 mL of 20% albumin, finding no significant difference between the two groups with respect to mortality. In 2015, the ALBIOS study [16] compared patient groups administered crystalloids alone and crystalloids plus 20% albumin and found no significant mortality difference.

A metanalysis comprising 90 studies involving adult patients revealed that every 1 g/dL decrease in serum albumin led to a 137% increase in mortality as well as a 28% and 71% increase in the durations of ICU and hospital stay, respectively [17].

The limitations of the present study include having a single-center and retrospective design and involving a heterogeneous patient population.

Conclusion

Serum albumin level is a simple, sensitive, specific, and low-cost marker used in most PICUs; we therefore suggest that it has an important prognostic value in this setting.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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